



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0146]

Guidance for Industry on Irritable Bowel Syndrome--Clinical Evaluation of Drugs for Treatment; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Irritable Bowel Syndrome--Clinical Evaluation of Drugs for Treatment.” This guidance is intended to assist the pharmaceutical industry and investigators who are developing drugs for the treatment of irritable bowel syndrome (IBS), specifically the IBS indications for IBS with diarrhea (IBS-D) and IBS with constipation (IBS-C). The guidance describes the evolution of patient-reported outcome (PRO) measures as primary endpoints for IBS clinical trials, and sets forth provisional endpoints and trial design recommendations that sponsors may apply to IBS clinical trials as PRO measurements continue to evolve. The guidance also discusses the future development of IBS PRO instruments. This guidance finalizes the draft guidance published in March 2010.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one

self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the guidance to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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301-796-0910.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Irritable Bowel Syndrome--Clinical Evaluation of Drugs for Treatment.” This guidance is intended to assist the pharmaceutical industry and investigators who are developing drugs for the treatment of IBS. This guidance applies to the IBS indications for IBS-D and IBS-C.

A well-defined and reliable PRO instrument that measures the clinically important signs and symptoms associated with each IBS subtype would be the ideal primary efficacy assessment tool in clinical trials used to support labeling claims, but at this time such an instrument is not available. We recognize that it will take some time to develop adequate instruments and that in

the meantime there is a great need to develop effective therapies for patients with IBS.

Therefore, until the appropriate PRO instruments have been developed, sponsors should consider the provisional endpoints and trial design recommendations set forth in the guidance.

This guidance was published as a draft guidance in March 2010. Changes made to the guidance took into consideration written and verbal comments received. In addition to editorial changes primarily for clarification, the major changes are as follows:

- The section on trial design was modified by adding a randomized withdrawal design to address the need for maintenance treatment to prevent sign or symptom recurrence.
- The section on trial endpoints was modified to note that a drug can be specifically developed to treat only one of two major signs or symptoms of IBS (abnormal defecation or abdominal pain). Demonstration of significant and clinically meaningful changes in the targeted single endpoint could serve as a basis for approval, as long as the other important symptom or sign has not worsened on treatment.
- Trial entry criteria for IBS-D were modified to allow more IBS-D patients to participate in IBS clinical trials, and the definition of a responder to treatments for IBS-D was modified accordingly.
- Definitions of a responder for abdominal pain alone, constipation, and diarrhea were added.
- The use of a daily responder analysis for IBS-D as a primary analysis was included.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on the clinical evaluation of drugs for the treatment of IBS. It does not create or confer any rights for or on any

person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

## II. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

## III. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: May 23, 2012.

Leslie Kux,

Assistant Commissioner for Policy.